ZYNLONTA® (loncastuximab tesirine-lpyl) – Use in Patients with Prior Chimeric Antigen Receptor T-cell (CAR-T) Therapy

Summary

- LOTIS-1 was a Phase 1, open-label, single-arm, multicenter study which evaluated the safety and tolerability of ZYNLONTA monotherapy in 183 adult patients (≥ 18 years of age) with relapsed or refractory (R/R) B-Cell Non-Hodgkin Lymphoma (B-NHL).[2]
    - Three patients (1.6%) had received prior chimeric antigen receptor T-cell (CAR-T) therapy and 2 (1.4%) of those patients were diagnosed with diffuse large B-cell lymphoma (DLBCL).[2]
        - Safety and efficacy in these subgroups were not reported.
- LOTIS-2 was a pivotal Phase 2, open-label, single-arm, multicenter study which evaluated the efficacy and safety of ZYNLONTA monotherapy in 145 patients (≥18 years of age) with R/R DLBCL following ≥2 lines of prior systemic therapy.[3]
    - Data from the 2-year follow-up (Data Cut-Off September 15, 2022) may differ from those in the LOTIS-2 primary analysis (Data Cut-Off April 6, 2020).
    - Fourteen patients (9.7%) had received prior CAR-T therapy and the ORR for this subgroup was 42.9% (n=6) (95% CI: 17.7, 71.1), with a CRR of 21.4% (n=3) (95% CI: 4.7, 50.8).[4]
    - Amongst the patients with prior CAR-T therapy, the median overall survival (OS) was 8.2 months (95% CI: 144 days, not reached), median progression free survival (PFS) was 1.4 months (95% CI: 21 days, not reached), and median duration of response (DoR) was 8 months (95% CI: 103 days, not reached).[1]

Background

- LOTIS-1 was a Phase 1, open-label, single-arm, multicenter study which evaluated the safety and tolerability of ZYNLONTA monotherapy in 183 adult patients with R/R B-NHL. The study was conducted in two parts, dose-escalation (Part 1) followed by dose-expansion (Part 2).[2]
    - Male or female patients (≥18 years of age) with histologically confirmed R/R B-NHL were enrolled if they failed or became intolerant to established therapies or if they had no other treatment options available.[2]
- LOTIS-2 was a pivotal Phase 2, open-label, single-arm, multicenter study which evaluated the efficacy and safety of ZYNLONTA monotherapy in 145 male or female patients (≥18 years of age) with R/R DLBCL following ≥2 lines of prior systemic therapy.[3]

Clinical Data

LOTIS-1 (Phase 1)

- Three patients (1.6%) had received prior CAR-T therapy and 2 (1.4%) of those patients were diagnosed with DLBCL.[2]
    - Safety and efficacy in these subgroups were not reported.
- In the overall population, the ORR in evaluable patients (n=180) was 45.6% (n=82) (95% CI: 38.1, 53.1), including a CRR of 26.7% (n=48) and a partial response rate (PRR) of 18.9% (n=34).[2]

LOTIS-2 (Phase 2)

- Data from the 2-year follow-up (Data Cut-Off September 15, 2022) may differ from those in the LOTIS-2 primary analysis (Data Cut-Off April 6, 2020). No new safety signals were identified during the long-term follow-up.
- In the updated results from the final 2-year data cut-off, the overall response rate (ORR) by central review was 48.3% (n=70), with a complete response rate (CRR) of 24.8% (n=36) and a partial response (PR) of 23.4% (n=34).[4]
- Fourteen patients (9.7%) had received prior CAR-T therapy and the ORR for this subgroup was 42.9% (n=6) (95% CI: 17.7, 71.1), with a CRR of 21.4% (n=3) (95% CI: 4.7, 50.8).[4]
    - Patients who had received previous CD19-directed therapy, including CAR-T therapy, were required to have a biopsy showing CD19 expression prior to starting ZYNLONTA.[3]
        - No prior CAR-T patients who were screened, failed due to a lack of CD19.[1]
    - Seven patients received axicabtagene ciloleucel, 2 patients received lisocabtagene maraleucel, and 4 received investigational CAR-T cell products. These investigational CAR-T cells included 2 anti-CD19 products, and 2 dual targeting agents, one directed against CD19/20 and another against CD19/CD22.[1]
    - In 10 patients ZYNLONTA was the first treatment after CAR-T.[1]
- Amongst the patients with prior CAR-T therapy (n=14), the median OS was 8.2 months (95% CI: 144 days, not reached), median PFS was 1.4 months (95% CI: 21 days, not reached), and median DoR was 8 months (95% CI: 103 days, not reached).[1,4]
- A total of 143 patients (98.6%) experienced at least one treatment-emergent adverse event (TEAE); most common Grade ≥3 TEAEs included neutropenia in 37 patients (26%), thrombocytopenia in 26 patients (18%), increased gamma-glutamyltransferase (GGT) in 24 patients (17%). Anemia was also reported in 15 patients (10.3%).[3]
    - TEAE analysis specifically for the 14 patients (9%) who had received prior CAR-T therapy was not conducted.

Literature Search

- A PubMed biomedical literature search conducted on November 22, 2024, yielded no further relevant information regarding the use of prior CAR-T therapy in patients receiving ZYNLONTA.

Relevant Prescribing Information

Section 14: Clinical Studies[5]

14.1: Relapsed or Refractory Diffuse Large B-Cell Lymphoma

- Of the 145 patients enrolled, the median age was 66 years (range 23 to 94), 59% male, and 94% had an ECOG performance status of 0 to 1. Race was reported in 97% of patients; of these patients, 90% were White, 3% were Black, and 2% were Asian. The diagnosis was DLBCL not otherwise specified (NOS) in 88% (including 20% with DLBCL arising from low-grade lymphoma), high-grade B-cell lymphoma in 7%. The median number of prior therapies was 3 (range 2 to 7), 63% with refractory disease, 17% with prior stem cell transplant, and 9% with prior chimeric antigen receptor (CAR) T-cell therapy.

References

[1] Caimi PF, Ardeshna KM, Reid E, et al. The antiCD19 antibody drug immunoconjugate loncastuximab achieves responses in DLBCL relapsing after antiCD19 CAR-T cell therapy. *Clin Lymphoma Myeloma Leuk*. 2021;S2152-2650(21)02437-X. doi:10.1016/j.clml.2021.11.005

[2] Hamadani M, Radford J, Carlo-Stella C, et al. Final results of a phase 1 study of loncastuximab tesirine in relapsed/refractory B-cell non-Hodgkin lymphoma. *Blood*. 2021;137(19):2634-2645. doi:10.1182/blood.2020007512

[3] Caimi PF, Ai W, Alderuccio JP, et al. Loncastuximab tesirine in relapsed or refractory diffuse large B-cell lymphoma (LOTIS-2): a multicentre, open-label, single-arm, phase 2 trial. *Lancet Oncol*. 2021;22(6):790-800 doi:10.1016/S1470-2045(21)00139-X

[4] Caimi PF, Ai WZ, Alderuccio JP, et al. Loncastuximab tesirine in relapsed/refractory diffuse large B-cell lymphoma: long-term efficacy and safety from the phase 2 LOTIS-2 study. Haematol. Published online August 31, 2023. doi: 110.3324/haematol.2023.283459

[5] ZYNLONTA® (loncastuximab tesirine-lpyl) FDA-approved Prescribing Information. October 2022.

ADC Therapeutics encourages all health care professionals to report any adverse events and product quality complaints to medical information at 855-690-0340. Please consult the ZYNLONTA Prescribing Information.